General

Guideline Title

Management of lung cancer. A national clinical guideline.

Bibliographic Source(s)

Scottish Intercollegiate Guidelines Network (SIGN). Management of lung cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2014 Feb. 67 p. (SIGN publication; no. 137). [318 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with lung cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2005 Feb. 63 p. (SIGN publication; no. 80). [345 references]

Any updates to the guideline in the interim period will be noted on the Scottish Intercollegiate Guidelines Network (SIGN) Web site .

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- December 14, 2016 – General anesthetic and sedation drugs : The U.S. Food and Drug Administration (FDA) is warning that repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children's brains. Consistent with animal studies, recent human studies suggest that a single, relatively short exposure to general anesthetic and sedation drugs in infants or toddlers is unlikely to have negative effects on behavior or learning. However, further research is needed to fully characterize how early life anesthetic exposure affects children's brain development.

Recommendations

Major Recommendations

Note from the Scottish Intercollegiate Guidelines Network (SIGN) and National Guideline Clearinghouse (NGC): In addition to these evidence-based recommendations, the guideline development group also identifies points of best clinical practice in the full-text guideline document.

The grades of recommendations (A-D) and levels of evidence (1++, 1+, 1-, 2++, 2+, 2-, 3, 4) are defined at the end of the "Major Recommendations" field.

Smoking

B - Advise patients to stop smoking as soon as the diagnosis of lung cancer is suspected and explain the benefits of doing so.

B - Inform patients that smoking increases the risk of pulmonary complications.

D - Do not postpone surgery for lung cancer to allow patients to stop smoking.

Diagnostic Investigations

Imaging

Chest X-Ray

D - A chest X-ray should be performed on all patients being investigated for the possibility of lung cancer.

Computed Tomography (CT) Scanning

B - Contrast enhanced CT scanning of the chest and abdomen is recommended in all patients with suspected lung cancer, regardless of chest X-ray results.

D - A tissue diagnosis should not be inferred from CT appearances alone.

D - Contrast enhanced CT scanning of the chest and abdomen should be performed prior to further diagnostic investigations, including bronchoscopy, and the results used to guide the investigation that is most likely to provide both a diagnosis and stage the disease to the highest level.

Positron Emission Tomography-Computed Tomography (PET-CT) Scanning

C - Fluorodeoxyglucose (FDG) PET-CT scanning may be used to investigate patients presenting with solitary lung lesions but histological/cytological confirmation of results will still be required.

Bronchoscopy

Central Tumors

B - Patients with central lesions who are otherwise fit should undergo flexible bronchoscopy in order to establish a histological or cytological diagnosis.

B - Visible tumours should be sampled using more than one technique to optimise sensitivity.

Peripheral Tumors

B - Bronchoscopy may provide a diagnosis for peripheral lesions, although percutaneous fine needle aspiration (FNA) biopsy is the preferred approach.

Percutaneous FNA Biopsy

B - Percutaneous FNA biopsy should be considered as the preferred diagnostic technique in patients with peripheral lesions.

Sputum Cytology

D - Sputum cytology should only be used in patients with large central lesions, where bronchoscopy or other diagnostic tests are deemed unsafe.

Advanced Bronchoscopic Techniques

Peripheral Lung Lesions

B - The use of advanced bronchoscopic techniques should be considered in patients with tumours where sampling with traditional approaches has failed to provide suitable diagnostic material.

Video-Assisted Thoracoscopy (VATS)

D - Thoracoscopy should be considered for patients with pleural effusions or peripheral lesions where less invasive means have not achieved histological and cytological confirmation of diagnosis.

Applicability of Cytological Samples for Optimal Assessment

B - Cytology samples can be used to provide material suitable for both non-small cell lung cancer (NSCLC) subtyping and some molecular analysis, provided the samples are appropriately handled and processed.

Staging Investigations

T-Stage in NSCLC

CT Scanning

B - Patients with suspected T3 or T4 disease who are otherwise fit for surgery should not be denied surgical exploration on the basis of a CT scan alone.

Magnetic Resonance Imaging (MRI) Scanning

B - MRI is not recommended in the routine assessment of the T stage except in patients with superior sulcus tumours. It may be of value in selected patients with suspected mediastinal invasion.

Thoracoscopy

C - Thoracoscopy may be considered for more accurate determination of the T stage in patients with suspected mediastinal or chest wall invasion when less invasive techniques have been inconclusive.

N Stage in NSCLC

CT Scanning of Mediastinal Nodes (N2/3)

B - A positive CT scan result for mediastinal lymphadenopathy (>10 mm in short axis diameter) indicates the need for pathological sampling of the enlarged nodes (with the exception of extensive infiltrating disease) if clinically indicated.

MRI Scanning of Mediastinal Nodes (N2/3)

B - MRI has no role in the routine staging of mediastinal lymphadenopathy.

PET Scanning of Mediastinal Nodes (N2/3)

B - All patients with NSCLC who are being considered for radical treatment should have a staging FDG PET-CT scan before treatment.

B - Patients with a negative FDG PET-CT scan result of mediastinal nodes of 10 mm or less in short axis on CT scanning could proceed to radical treatment.

B - Histological confirmation of mediastinal nodes should be considered if nodes are >10 mm in short axis diameter on CT or nodes are positive on PET-CT scanning.

Neck Ultrasonography FNA

D - Neck ultrasound FNA should be considered for a pathological diagnosis and staging in the case of a positive supraclavicular node on clinical examination, by CT or PET-CT scanning.

Endoscopic Sampling of the Mediastinal Lymph Nodes

A - Endoscopic assessment of the mediastinal lymph nodes with endobronchial ultrasound fine-needle aspiration (EBUS-FNA) with or without endoscopic ultrasound FNA (EUS-FNA) should be offered to patients with suspected lung cancer prior to mediastinoscopy.

M Stage in NSCLC

Clinical Evaluation

C - Patients with clinical stage I or II disease on the basis of a CT scan of the chest and abdomen, PET-CT and a negative clinical evaluation do not require further investigation to look for extrathoracic metastases.

Pleural Effusion

D - In patients being considered for active therapy, pleural effusion should be investigated with pleural aspiration and/or pleural biopsy using image guided or thoracoscopic biopsy.

D - The presence of malignant cells is required to categorise the lesion as M1a.

FDG-PET CT Scanning and Detection of Distant Metastases

C - All patients with NSCLC who are being considered for radical treatment should have a staging PET-CT scan to detect occult distant metastases.

Brain Metastases

C - Contrast-enhanced head CT or MRI in asymptomatic patients with clinical stage I-II disease is not recommended.

Bone Metastases

B - A positive nuclear bone scan in patients with otherwise potentially curable disease should be confirmed by other studies (e.g., plain X-rays, MRI or biopsy).

Liver Metastases

C - Ultrasound (US), contrast enhanced CT, FDG PET-CT or MRI can be used to characterise most benign focal hepatic abnormalities >10 mm.

C - A definitive confirmation of a liver metastasis can only be made by needle biopsy.

C - The management of patients with lesions too small to characterise by imaging and not amenable to biopsy is best guided by an estimation of the chance of metastatic disease given the clinical stage and symptoms.

Adrenal Gland Metastases

B - A negative FDG PET-CT reliably excludes adrenal metastases.

B - In patients with PET-CT positive adrenal lesions pathology, confirmation may be considered unless there is overwhelming clinical and imaging evidence of widespread metastatic disease.

D - In patients with indeterminate adrenal lesions on FDG PET-CT further assessment with adrenal specific CT or MRI criteria may be considered. If noninvasive imaging findings are indeterminate, adrenal sampling such as EUS-FNA, percutaneous biopsy or adrenalectomy may be considered.

Lung Metastases

C - Patients with small pulmonary nodules should not be denied a curative approach without a definitive diagnosis (by biopsy, FNA or wedge resection).

Small Cell Lung Cancer (SCLC)

B - Investigation for distant metastases is recommended when intensive treatment is being considered for patients with SCLC who are considered to be at high risk of having distant metastases.

Surgery

NSCLC

Radical Surgery (Stage I and II)

D - Patients with stage I and II NSCLC should be considered for curative surgery whenever possible.

Reduction of Surgical Morbidity and Mortality

D - Lung resection should be as limited as possible without compromising cancer clearance. Lobectomy remains the procedure of choice for fit patients.

D - Every effort should be made to avoid a thoracotomy that does not progress to a lung resection.

Video-Assisted Thoracoscopic Surgery (Stage I)

B - Video-assisted thoracoscopic surgical resection may be offered to patients with clinical stage I NSCLC lung cancer.

Mediastinal Lymph Node Management of Patients with NSCLC

B - Systematic nodal dissection should be undertaken for lymph node management at resection. Simple nodal sampling is not adequate and radical mediastinal lymphadenectomy is not necessary.

SCLC

Effectiveness of Surgery

A - Routine surgery for limited disease SCLC is not recommended.

D - Patients with early stage SCLC may be considered for resection following extensive staging investigation.

Radiotherapy

NSCLC

Radical Radiotherapy (Stage I and II)

B - Patients with NSCLC stage I and II who are medically inoperable or who do not consent to surgery should be offered radical radiotherapy.

Hyperfractionated and/or Accelerated Radiotherapy (Stage III)

A - Patients having radical radiotherapy should be given continuous, hyperfractionated, accelerated radiotherapy (CHART) (54 Gy in 36 fractions over 12 days) in preference to 60 Gy in 30 fractions over six weeks.

Stereotactic Radiotherapy

B - Patients with early-stage peripheral lung cancers who are not suitable for surgery should be considered for stereotactic ablative radiotherapy.

Radical Radiotherapy in Patients with NSCLC

D - A clinical oncologist specialising in lung oncology should determine suitability for radical radiotherapy, taking into account performance status and comorbidities.

D - Perform spirometry in all patients being considered for treatment with curative intent. Measure carbon monoxide transfer factor (TLCO) if breathlessness is disproportionate or there is other lung pathology.

Palliative Thoracic Radiotherapy in Patients with Symptomatic, Locally Advanced Lung Cancer

A - Patients with thoracic symptoms and good performance status not suitable for radical radiotherapy should be considered for more fractionated, higher dose regimens of palliative radiotherapy, such as 39 Gy in 13 fractions.

A - Patients with thoracic symptoms and poor performance status not suitable for radical radiotherapy should receive palliative radiotherapy.

Radiotherapy in Patients with SCLC and NSCLC Brain Metastases

Radiotherapy in Patients with Isolated Brain Metastases

B - Patients with single brain metastases should be offered resection followed by adjuvant radiotherapy.

Prophylactic Cranial Irradiation in Patients with SCLC and Limited Disease

A - Prophylactic cranial irradiation should be offered to patients with limited disease SCLC achieving remission after systemic anticancer therapy.

Prophylactic Cranial Irradiation in SCLC Patients with Extensive Disease

A - Prophylactic cranial irradiation should be offered to patients with extensive stage small cell lung cancer who have demonstrated a response to systemic anticancer therapy. Patients should be informed of the potential prolongation of treatment-related side effects (hair loss and fatigue) as well as decreased functioning scales to allow informed treatment decisions to be made.

Palliative Radiotherapy in Patients with Symptomatic Metastases

A - Patients with lung cancer and symptomatic bone metastases should be treated with a single 8 Gy fraction of palliative radiotherapy.

Systemic Anticancer Therapy (SACT)

First Line Therapy for Patients with Stage IIIB and IV NSCLC

A - First line single agent tyrosine kinase inhibitors (TKI) should be offered to patients with advanced NSCLC who have a sensitising epidermal growth factor receptor (*EGFR*) mutation. Adding combination SACT to a TKI confers no benefit and should not be used.

A - Patients who have advanced disease, are performance status 0-1, have predominantly nonsquamous NSCLC and are *EGFR* mutation negative should be offered combination SACT with cisplatin and pemetrexed.

A - All other patients with NSCLC should be offered combination SACT with cisplatin/carboplatin and a third generation agent (docetaxel, gemcitabine, paclitaxel or vinorelbine).

A - Platinum doublet SACT should be given in four cycles; it is not recommended that treatment extends beyond six cycles.

Second Line Therapy

A - Second line systemic anticancer therapy with single agent docetaxel or erlotinib should be considered for patients with performance status 0-2 recurrent NSCLC who have been previously treated with first line systemic anticancer therapy for advanced disease.

A - Second line systemic anticancer therapy with pemetrexed should be considered for patients with advanced non-squamous cell NSCLC who have been previously treated with first line systemic anticancer therapy for advanced disease.

Postoperative Systemic Anticancer Therapy

A - Patients with good performance status (PS 0-1) who have completely resected NSCLC (stage II to IIIa) should be offered platinum based postoperative systemic anticancer therapy.

Systemic Anticancer Therapy for Patients with SCLC

Systemic Anticancer Therapy in Older Patients

A - Combination intravenous systemic anticancer therapy should be considered for patients with SCLC over 70 years of age with performance status 0-2.

Standard Regimens

A - A regimen containing a platinum agent and etoposide is recommended for first line treatment of patients with SCLC.

Duration of Systemic Anticancer Therapy

A - In patients with SCLC the recommended number of systemic anticancer therapy cycles is three to six.

Second Line Systemic Anticancer Therapy

B - Second line systemic anticancer therapy in patients with SCLC should be considered depending on the duration of response to first line treatment and on patients' performance status and wishes.

Maintenance

B - Maintenance systemic anticancer therapy following first line treatment is not recommended.

Combined Modalities

Postoperative (Adjuvant) Radiotherapy in Patients with NSCLC Undergoing Curative Surgery

A - Patients with NSCLC who have had complete tumour resection should not receive postoperative radiotherapy, except as part of a randomised trial.

Concurrent Chemoradiotherapy in Patients with NSCLC

A - Concurrent chemoradiotherapy should be administered to patients with locally advanced NSCLC (suitable for radical radiotherapy) who have a good performance status (PS 0-1).

Palliative Interventions

Management of Malignant Pleural Effusion

A - Talc is the optimal sclerosant for thoracoscopic pleurodesis in patients with a malignant pleural effusion who are fit enough to undergo sedation or general anaesthesia.

Management of Superior Vena Cava Obstruction

Stenting

B - In patients with superior vena cava obstruction due to SCLC, systemic anticancer therapy/radiotherapy is recommended as initial treatment, but stenting may be considered for relapse or persistent superior vena cava obstruction.

Management of Bone Metastases

Bisphosphonates

B - Patients with lung cancer who have symptomatic bone metastases should be considered for treatment with a bisphosphonate.

Supportive and Palliative Care

Specialist Palliative Care Services

B - All patients with lung cancer should have access to a specialist palliative care team.

Symptom Management

D - Symptoms should be assessed regularly and appropriate interventions initiated by the full multidisciplinary team.

Multidisciplinary Teams, Follow Up and Communication

Role of the Multidisciplinary Team

D - All patients with a diagnosis of lung cancer should have their treatment and management planned and directed by a multidisciplinary team.

D - Allied health professional services should be offered to all patients with lung cancer.

Follow Up

B - Follow up by clinical nurse specialists should complement conventional arrangements.

B - Hospital follow up should be continued where hospital treatment or specialist advice is still required, or whilst clinical trials are ongoing.

- After surgery, the surgeon should follow up all patients initially: later follow up should be according to local policy.
- After palliative therapy is completed, follow up should be agreed between the oncologist, respiratory physician, general practitioner (GP) and palliative care team.

Communication

A - Communication skills training should be provided across the multidisciplinary team.

Definitions:

Levels of Evidence

1++: High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+: Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias

1-: Meta-analyses, systematic reviews, or RCTs with a high risk of bias

2++: High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+: Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2-: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3: Non-analytic studies (e.g., case reports, case series)

4: Expert opinion

Grades of Recommendation

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A: At least one meta-analysis, systematic review, or RCT rated as 1++ and directly applicable to the target population; *or*

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 1++ or 1+

C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 2++

D: Evidence level 3 or 4; *or*

Extrapolated evidence from studies rated as 2+

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Lung cancer:

- Small cell lung cancer (SCLC)
- Non-small cell lung cancer (NSCLC)

Note: The guideline does not address other thoracic malignant disease such as mesothelioma, carcinoma in situ or secondary cancers that have spread to the lungs.

Other Disease/Condition(s) Addressed

- Metastatic disease
- Tobacco dependence
- Vena cava obstruction

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Oncology

Pathology

Pulmonary Medicine

Radiation Oncology

Thoracic Surgery

Intended Users

Advanced Practice Nurses

Allied Health Personnel

Nurses

Patients

Pharmacists

Physician Assistants

Physicians

Public Health Departments

Guideline Objective(s)

To cover all aspects of the management of patients with small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) and to provide information for discussion with patients and carers

Note: Strategies for primary prevention or screening are outwith the remit of the guideline. The guideline does not address the public health issues associated with smoking.

Target Population

Patients with suspected or confirmed small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC)

Interventions and Practices Considered

Diagnosis/Evaluation

1. Imaging including chest X-ray, computed tomography (CT) scanning, fluorodeoxyglucose-positron emission tomography (FDG-PET) scanning
2. Bronchoscopy
3. Percutaneous fine needle aspiration (FNA) biopsy
4. Sputum cytology
5. Video-assisted thoracoscopy (VATS)
6. Use of cytology samples to provide material suitable for both non-small cell lung cancer (NSCLC) subtyping and molecular analysis
7. Staging:
    - T stage in NSCLC via CT scanning, magnetic resonance imaging (MRI) scanning, and thoracoscopy
    - N stage in NSCLC via CT scanning, MRI, mediastinoscopy, FDG-PET scanning of mediastinal nodes, neck ultrasound FNA, endoscopic sampling of the mediastinal lymph node
    - M stage in NSCLC via clinical evaluation, investigation of pleural effusion, FDG-PET scanning and other imaging investigations for detection of metastases (distant, brain, bone, liver, adrenal gland, lung)
    - Small cell lung cancer (SCLC)

Management/Treatment

1. Advising patients to quit smoking as soon as diagnosis of lung cancer is suspected
2. Surgery for NSCLC:
    - Radical surgery for stage I and II
    - Reduction of surgical morbidity and mortality
    - VATS (for stage I)
    - Mediastinal lymph node dissection
3. Resection for early stage SCLC following extensive staging (routine surgery for limited disease SCLC is not recommended)
4. Radiotherapy:
    - Radical radiotherapy (stage I and II NSCLC)
    - Hyperfractionated and/or accelerated radiotherapy (stage III NSCLC)
    - Stereotactic radiotherapy
    - Palliative thoracic radiotherapy for symptomatic, locally advanced lung cancer
    - Radiotherapy for brain metastases of SCLC and NSCLC
    - Prophylactic cranial irradiation for SCLC and limited or extensive disease
    - Palliative radiotherapy for symptomatic metastases
5. First line systemic anticancer therapy (SACT) for NSCLC:
    - Single agent tyrosine kinase inhibitors (TKI)
    - Combination cisplatin and pemetrexed
    - Cisplatin/carboplatin and a third generation agent (docetaxel, gemcitabine, paclitaxel or vinorelbine)
6. Second line SACT for NSCLC:
    - Single agent docetaxel or erlotinib
    - Pemetrexed
7. Postoperative platinum-based systemic anticancer therapy for NSCLC
8. First line SACT with a regimen containing a platinum agent and etoposide for SCLC (maintenance therapy following is not recommended)
9. Second line chemotherapy in patients with SCLC if indicated
10. Combined modalities including:
    - Postoperative (adjuvant) radiotherapy
    - Concurrent chemotherapy in NSCLC patients undergoing radical radiotherapy
11. Palliative interventions:
    - Talc for malignant pleural effusion
    - Endovascular stenting for superior vena cava obstruction due to SCLC
    - Bisphosphonates for symptomatic bone metastases
12. Supportive and palliative care:
    - Ensuring access to a specialist palliative care team

    - Regular symptom assessment and appropriate interventions by full multidisciplinary team
13. Implementation of a multidisciplinary team
14. Allied health professional services offered to patients
15. Follow-up and communication with patients

Major Outcomes Considered

- Sensitivity and specificity of diagnostic tests
- Incidence and severity of complications
- Objective response rates to treatment
- Survival rates (2-year, 5-year, median, progression-free, overall)
- Pulmonary function
- Quality of Life
- Toxicity
- Pain control
- Recovery from procedure(s)

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Systematic Literature Review

The evidence base for this guideline was synthesised in accordance with Scottish Intercollegiate Guidelines Network (SIGN) methodology. A systematic review of the literature was carried out using an explicit search strategy (see the "Availability of Companion Documents" field) devised by a SIGN Evidence and Information Scientist. Databases searched include MEDLINE, EMBASE, CINAHL, PsycINFO and the Cochrane Library. The year range covered was 2005 to 2012. Internet searches were carried out on various websites including the US National Guideline Clearinghouse (NGC). The main searches were supplemented by material identified by individual members of the development group. Each of the selected papers was evaluated by two members of the group using standard SIGN methodological checklists before conclusions were considered as evidence.

Literature Search for Patient Issues

At the start of the guideline development process, a SIGN Evidence and Information Scientist conducted a literature search for qualitative and quantitative studies that addressed patient issues of relevance to patients with lung cancer. Databases searched include MEDLINE, EMBASE, CINAHL, and PsycINFO, and the results were summarised by the SIGN Patient Involvement Officer and presented to the guideline development group.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Levels of Evidence

1++: High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias

1+: Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias

1-: Meta-analyses, systematic reviews, or RCTs with a high risk of bias

2++: High quality systematic reviews of case control or cohort studies

High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal

2+: Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal

2-: Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal

3: Non-analytic studies (e.g., case reports, case series)

4: Expert opinion

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Once papers have been selected as potential sources of evidence, the methodology used in each study is assessed to ensure its validity. The result of this assessment will affect the level of evidence allocated to the paper, which will in turn influence the grade of recommendation that it supports.

The methodological assessment is based on a number of key questions that focus on those aspects of the study design that research has shown to have a significant influence on the validity of the results reported and conclusions drawn. These key questions differ between study types, and a range of checklists is used to bring a degree of consistency to the assessment process. Scottish Intercollegiate Guidelines Network (SIGN) has based its assessments on the MERGE (Method for Evaluating Research and Guideline Evidence) checklists developed by the New South Wales Department of Health, which have been subjected to wide consultation and evaluation. These checklists were subjected to detailed evaluation and adaptation to meet SIGN's requirements for a balance between methodological rigour and practicality of use.

The assessment process inevitably involves a degree of subjective judgment. The extent to which a study meets a particular criterion - e.g., an acceptable level of loss to follow up - and, more importantly, the likely impact of this on the reported results from the study will depend on the clinical context. To minimise any potential bias resulting from this, each study must be evaluated independently by at least two group members. Any differences in assessment should then be discussed by the full group. Where differences cannot be resolved, an independent reviewer or an experienced member of SIGN Executive staff will arbitrate to reach an agreed quality assessment.

Evidence Tables

Evidence tables are compiled by SIGN executive staff based on the quality assessments of individual studies provided by guideline development group members. The tables summarise all the validated studies identified from the systematic literature review relating to each key question. They are presented in a standard format to make it easier to compare results across studies, and will present separately the evidence for each outcome measure used in the published studies. These evidence tables form an essential part of the guideline development record and ensure that the basis of the guideline development group's recommendations is transparent.

Additional details can be found in the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50]), available from the SIGN Web site .

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Synthesising the Evidence

Guideline recommendations are graded to differentiate between those based on strong evidence and those based on weak evidence. This judgement is made on the basis of an (objective) assessment of the design and quality of each study and a (perhaps more subjective) judgment on the consistency, clinical relevance and external validity of the whole body of evidence. The aim is to produce a recommendation that is evidence-based, but which is relevant to the way in which health care is delivered in Scotland and is therefore implementable.

It is important to emphasise that the grading does not relate to the importance of the recommendation, but to the strength of the supporting evidence and, in particular, to the predictive power of the study designs from which that data was obtained. Thus, the grading assigned to a recommendation indicates to users the likelihood that, if that recommendation is implemented, the predicted outcome will be achieved.

Considered Judgement

It is rare for the evidence to show clearly and unambiguously what course of action should be recommended for any given question. Consequently, it is not always clear to those who were not involved in the decision making process how guideline developers were able to arrive at their recommendations, given the evidence they had to base them on. In order to address this problem, Scottish Intercollegiate Guidelines Network (SIGN) has introduced the concept of considered judgement.

Under the heading of considered judgement, guideline development groups summarise their view of the total body of evidence covered by each evidence table.

Each guideline group considers the following factors:

- Quantity, quality, and consistency of evidence
- External validity (generalisability) of studies
- Directness of application to the target population for the guideline
- Any evidence of potential harms associated with implementation of a recommendation
- Clinical impact (i.e., the extent of the impact on the target patient population, and the resources needed to treat them in accordance with the recommendation)
- Whether, and to what extent, any equality groups may be particularly advantaged or disadvantaged by the recommendations made
- Implementability (i.e., how practical it would be for the National Health Service (NHS) Scotland to implement the recommendation)

Then the group is asked to summarise its view on all of these issues, both the quality of the evidence and its potential impact, before making a graded recommendation. This summary should be succinct, and taken together with its views of the level of evidence represent the first draft of the text that will appear in the guideline immediately before a graded recommendation.

Additional detail about SIGN's process for formulating guideline recommendations is provided in Section 7 of the companion document titled "SIGN 50: A Guideline Developers' Handbook." (Edinburgh [UK]: Scottish Intercollegiate Guidelines Network. [SIGN publication; no. 50]), available from the SIGN Web site .

Rating Scheme for the Strength of the Recommendations

Grades of Recommendations

Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.

A: At least one meta-analysis, systematic review, or randomised controlled trial (RCT) rated as 1++ and directly applicable to the target population; *or*

A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results

B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results;

or

Extrapolated evidence from studies rated as 1++ or 1+

C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; *or*

Extrapolated evidence from studies rated as 2++

D: Evidence level 3 or 4; *or*

Extrapolated evidence from studies rated as 2+

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The national open meeting is the main consultative phase of Scottish Intercollegiate Guidelines Network (SIGN) guideline development.

Peer Review

All SIGN guidelines are reviewed in draft form by independent expert referees, who are asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. A number of general practitioners (GPs) and other primary care practitioners also provide comments on the guideline from the primary care perspective, concentrating particularly on the clarity of the recommendations and their assessment of the usefulness of the guideline as a working tool for the primary care team. The draft is also sent to at least two lay reviewers in order to obtain comments from the patient's perspective.

It should be noted that all reviewers are invited to comment as individuals, not as representatives of any particular organisation or group. Corporate interests, whether commercial, professional, or societal have an opportunity to make representations at the national meeting stage where they can send representatives to the meeting or provide comment on the draft produced for that meeting. Peer reviewers are asked to complete a declaration of interests form.

The comments received from peer reviewers and others are carefully tabulated and discussed with the Chair and with the guideline development group. Each point must be addressed and any changes to the guideline as a result noted or, if no change is made, the reasons for this recorded.

As a final quality control check prior to publication, the guideline and the summary of peer reviewers' comments are reviewed by the SIGN Editorial Group for that guideline to ensure that each point has been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. Each member of the guideline development group is then asked formally to approve the final guideline for publication.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of patients with lung cancer

Potential Harms

- Prophylactic cranial irradiation is associated with an increase in adverse effects, longer duration of hair loss and fatigue, and a small but negative impact on functioning scale.
- In patients with extensive disease small cell lung cancer (SCLC), careful patient selection is crucial to avoid unnecessary toxicity. Combination systemic anticancer therapy (SACT) has been shown to be less toxic and more effective than single agent treatment with oral etoposide.
- Percutaneous needle biopsy has an overall complication rate of 8% to 9% with 3% to 4% having major complications (e.g., pneumothorax or significant haemorrhage). There is a high false negative rate (25%) resulting in limited ability to confirm a benign diagnosis.
- Adult respiratory distress syndrome following talc pleurodesis has been reported as a complication in case reports but not in randomised controlled trials (RCTs).
- The main complications in the use of tunnelled pleural catheters appear to be blockage or dislodgement of the catheter, or seeding down the drain tract. In a retrospective audit, seeding affected 6.7% of 45 patients. Spontaneous pleuradhesis occurred in up to 25% of cases. Very few cases of pleural infection secondary to the drain have been reported.
- There is some evidence that concurrent chemoradiation increases toxicity in patients with limited disease SCLC.
- The PORT meta-analysis suggests an adverse effect of radiotherapy on survival with a hazard ratio of 1.21 (95% CI 1.08 to 1.34), favouring surgery; two year survival with adjuvant radiotherapy was 48% versus 50% in the surgery alone group.
- False positive and false negative rates of diagnostic test.

Contraindications

Contraindications

Bronchoscopy is contraindicated in patients with large central lesions.

Qualifying Statements

Qualifying Statements

- This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is, however, advised that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.
- Recommendations within this guideline are based on the best clinical evidence. Some recommendations may be for medicines prescribed outwith the marketing authorisation (MA) also known as product licence. This is known as 'off label' use.
  Medicines may be prescribed off label in the following circumstances:
    - For an indication not specified within the marketing authorization
    - For administration via a different route

- For administration of a different dose
- For a different patient population

An unlicensed medicine is a medicine which does not have MA for medicinal use in humans.

Generally 'off label' use of medicines becomes necessary if the clinical need cannot be met by licensed medicines within the marketing authorisation. Such use should be supported by appropriate evidence and experience.

"Prescribing medicines outside the conditions of their marketing authorisation alters (and probably increases) the prescribers' professional responsibility and potential liability."

The General Medical Council (GMC) recommends that when prescribing a medicine off-label, doctors should:

- Be satisfied that such use would better serve the patient's needs than an authorised alternative (if one exists).
- Be satisfied that there is sufficient evidence/experience of using the medicines to show its safety and efficacy, seeking the necessary information from appropriate sources.
- Record in the patient's clinical notes the medicine prescribed and, when not following common practice, the reasons for the choice.
- Take responsibility for prescribing the medicine and for overseeing the patient's care, including monitoring the effects of the medicine.

Non-medical prescribers should ensure that they are familiar with the legislative framework and their own professional prescribing standards.

Prior to any prescribing, the licensing status of a medication should be checked in the summary of product characteristics (SPC). The prescriber must be competent, operate within the professional code of ethics of their statutory body and the prescribing practices of their employer.

Implementation of the Guideline

Description of Implementation Strategy

Implementation of national clinical guidelines is the responsibility of each National Health Service (NHS) Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

Implementation of this guideline will be encouraged and supported by the Scottish Intercollegiate Guidelines Network (SIGN).

Implementation Tools

Mobile Device Resources

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Scottish Intercollegiate Guidelines Network (SIGN). Management of lung cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2014 Feb. 67 p. (SIGN publication; no. 137). [318 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1998 Feb (revised 2014 Feb)

Guideline Developer(s)

Scottish Intercollegiate Guidelines Network - National Government Agency [Non-U.S.]

Source(s) of Funding

Scottish Executive Health Department

Guideline Committee

Guideline Development Group

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Financial Disclosures/Conflicts of Interest

All members of the guideline development group made declarations of interest. A register of interests is available as a supplement in the supporting materials section on the Scottish Intercollegiate Guidelines Network (SIGN) Web site .

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with lung cancer. A national clinical guideline. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN); 2005 Feb. 63 p. (SIGN publication; no. 80). [345 references]

Any updates to the guideline in the interim period will be noted on the Scottish Intercollegiate Guidelines Network (SIGN) Web site .

Guideline Availability

Electronic copies: Available from the Scottish Intercollegiate Guidelines Network (SIGN) Web site .

Availability of Companion Documents

The following are available:

- Quick reference guide: Management of lung cancer. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network; 2014 Feb. 14 p. Electronic copies: Available in Portable Document Format (PDF) from the Scottish Intercollegiate Guidelines Network (SIGN) Web site .
- SIGN 50: A guideline developer's handbook. Edinburgh (Scotland): Scottish Intercollegiate Guidelines Network (SIGN publication; no. 50). Electronic copies: Available from the SIGN Web site .

The search strategy for the guideline update is available as a supplement in the supporting materials section on the SIGN Web site .

Executive summaries of SIGN guidelines are available for mobile devices through the guidelines app on the SIGN Web site .

Patient Resources

None available

NGC Status

This summary was completed by ECRI on February 6, 2002. The information was verified by the guideline developer as of April 9, 2002. The summary was updated on April 4, 2005. The summary was updated by ECRI Institute on April 4, 2014. The updated information was verified by the guideline developer on April 10, 2014. This summary was updated by ECRI Institute on July 18, 2014 following the U.S. Food and Drug Administration advisory on Docetaxel. This summary was updated by ECRI Institute on February 15, 2017 following the U.S. Food and Drug Administration advisory on general anesthetic and sedation drugs.

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